UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/721,550	11/22/2000	Norbert Reich	510015-234	3451

33717 7590 06/16/2003

GREENBERG TRAURIG LLP
2450 COLORADO AVENUE, SUITE 400E
SANTA MONICA, CA 90404

EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/721,550	REICH, NORBERT	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7,10-18,20,23,25,29,31,32,34,35 and 37-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7,10-18,20,23,25,29,31,32,34,35 and 37-40* is/are rejected.

7)☒ Claim(s) 32 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 10 & 20. Dec.02
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to papers filed 14 January 2003 in which claims 1, 16-18, 20, 22-23, 25, 29, 31, 34-35 and 39 were amended and claims 19, 22, 24, 26, 27 and 30 were canceled. It is noted that Claim 22 has been both canceled and amended. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action dated 17 September 2002 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection.

New grounds for rejection are discussed.

Claims 1, 4-7, 10-18, 20, 23, 25, 29, 31-32, 34-35 and 37-40 are under prosecution.

Claim Objections

2. Claim 32 is objected to because it depends from canceled Claim 22.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 is indefinite because the recitations "the multiple labeled probes" and "the multiplying of the labeled probes" lack proper antecedent basis in Claims 16, 17, 18, 10 and 22-25. It is suggested that Claim 32 be amended to provide proper antecedent basis.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1, 4, 7, 10, 31 and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Kurane et al (U.S. Patent No. 6,495,326, filed 20 April 2000).

The following claims are drawn to a substrate.

Regarding Claim 1, Kurane et al disclose the substrate having a surface area, the surface area comprising attached labeled probe molecules, said labeled probe molecules having therein incorporated nucleotide analogs that fluoresce and whose decrease in florescence when substantially approaching zero quantifies the presence or hybridization of complementary molecules to the labeled probe molecules by quenching a first florescence provided by the labeled probe molecules (Example 14, Column 35 and Fig. 6).

Regarding Claim 4, Kurane et al disclose the labeled probe comprises native and non-native nucleotides (Column 35, lines 11-16 and Example 5, Columns 27-28).

Regarding Claim 7, Kurane et al disclose the labeled probes are comprised of amino acids i.e. PNA (Column 9, lines 34-37).

Regarding Claim 10, Kurane et al disclose the substrate is a microarray divided into quadrants wherein each quadrant has a different labeled probe (Column 13, lines 19-46 and Fig. 6).

Regarding Claim 31, Kurane et al disclose a substrate having a surface area, the surface area comprising attached and quantified labeled probe molecules, said probe further comprising a fluorescent label, said fluorescent label including at least one nucleotide analog incorporated as part of a nucleotide sequence defining said labeled probe molecules (Example 5, Columns 27-28 and Example 14, Column 35).

Regarding Claim 38, Kurane et al disclose the substrate wherein the labeled probe fluoresces at a wavelength of about 300nm to about 700nm (Example 5, Column 28, line 35).

7. Claims 16, 17, 20, 23, 25, 29, 32 and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Kurane et al (U.S. Patent No. 6,495,326, filed 20 April 2000).

The following claims are drawn to a method for assessing the presence of a target molecule.

Regarding Claims 16, 17, 20, 23, 25, 29, 32 and 37, Kurane et al disclose a method for quantifying the amount of a target molecule in solution comprising the steps of: providing a first substrate having a surface area comprising a known number of labeled probe molecules, said labeled probe molecules include at least one nucleotide analog capable of fluorescence; detecting a first level of nucleotide analog fluorescence expressed by the labeled probe molecules on the first substrate; contacting the first substrate with a volume of sample containing unlabeled target nucleotide sequences; providing a sufficient condition and time for unlabeled target molecules to selectively pair with the labeled probe molecules; removing the first substrate and detecting the level of nucleotide analog fluorescence expressed by said known number of labeled probe molecules after exposure to the sample containing unlabeled target molecules; where the level of nucleotide analog fluorescence expression of the first substrate is substantially reduced to levels substantially similar to background levels, repeating the steps with subsequent substrates, having surface areas comprising known numbers of labeled probe molecules; and calculating the amount of target molecule in the volume of sample by adding the known clamber of labeled probe molecules present on the first substrate and subsequent substrates contacted with the sample, wherein the levels of nucleotide analog fluorescence expression of the substrates are reduced to a level approaching zero relative to the levels prior to contacting the sample. whereby said amount of target molecule is quantified (Column 12, lines 51-64; Column 15, lines 43-59; Example 5, Columns 27-28 and Example 14, Column 35) wherein the probes and primers are obtained by non-amplification (Examples 5-7).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 11-15, 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurane et al (U.S. Patent No. 6,495,326, filed 20 April 2000) in view of Fodor et al (U.S. Patent No. 5,800,992, issued 1 September 1998).

Regarding Claims 11-15, Kurane et al disclose the substrate having a surface area, the surface area comprising attached labeled probe molecules, said labeled probe molecules having therein incorporated nucleotide analogs that fluoresce and whose decrease in florescence when substantially approaching zero quantifies the presence or hybridization of complementary molecules to the labeled probe molecules by quenching a first florescence provided by the labeled probe molecules (Example 14, Column 35 and Fig. 6) wherein the probes are immobilized using well known techniques e.g. Fodor (Column 13, lines 29-46) but Kurane et al do not specifically teach probe density and/or bead substrates. However, the claimed probe densities and bead substrate were well known in the art at the time the claimed invention was made as taught by Fodor et al. Specifically, Fodor et al teach microarray substrates having from about 100 to about 10,000 different labeled probe (molecule) molecules located upon about 100 to about 10,000 different quadrants (Column 20, lines 20-39); having about 100 to

about 1,000 labeled probe molecules per quadrant (Column 20, lines 20-39); wherein the substrate is a bead, said bead sizes range from about 10 microns to about 20 microns (Column 71, lines 23-27); bead substrate of claimed wherein the bead is formed of a ferromagnetic fetal core and a polymeric coating (Column 21, lines 35-63 and Column 45, lines 63-67);having from about 100 to about 1,000 labeled probe molecules attached to the surface area of the bead (Column 71, lines 23-40). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the probe density of Fodor et al to the immobilized probes of Kurane et al to thereby provide the plurality of probes efficiently as taught by Fodor et al (Column 20, lines 40-53). Additionally, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the bead substrates of Fodor et al to the substrate of Kurane et al to thereby provide for target-bound bead sorting for the expected benefit of sorting targets from non-targets simply by applying a magnetic system (Fodor et al, column 21, lines 36-63).

Regarding Claim 18, Kurane et al teach the method of Claim 17 as detailed above but they do not teach the label is evaluated using a flow cytometer. However, flow cytometer label evaluation was well known in the art at the time the claimed invention was made as taught by Fodor et al who teach that using flow cytometry, the number of labeled beads is accurately determined (Column 71, lines 22-52). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the flow cytometer detection of Fodor et al to the label detection of Kurane et al for the expected benefit of accurately quantitating target molecules as taught by Fodor et al (Column 71, lines 22-52).

10. Claims 5-6, 34-35 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurane et al (U.S. Patent No. 6,495,326, filed 20 April 2000) in view of Hawkins (U.S. Patent No. 6,451,530, published 18 June 1998).

Regarding Claims 5-6 and 34-35, Kurane et al teach the substrate the of Claims 1 and 31 having a surface area, the surface area comprising attached labeled probe molecules, said labeled probe molecules having therein incorporated nucleotide analogs that fluoresce and whose decrease in florescence when substantially approaching zero quantifies the presence or hybridization of complementary molecules to the labeled probe molecules by quenching a first florescence provided by the labeled probe molecules (Example 14, Column 35 and Fig. 6) wherein the probes are labeled with nucleic acid analogs (Column 9, line 38-Column 10, line 10). Kurane et al do not teach the analogs are selected from the claimed analogs e.g. 2-amino purine. However, incorporation of 2-amino purine analogs into nucleic acid probes were well known in the art at the time the claimed invention was made as taught by Hawkins (Column 4, lines 44-54). Hawkins further teaches that fluorescent signals generated from probes comprising the 2-amino purine changes upon conformational change of the probe (Column 3, lines 26-36). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the analog of Kurane et al with the 2-amino purine of Hawkins based on the teaching of Hawkins wherein conformational change produces a change in signal (Abstract).

Regarding Claim 40, Kurane et al teach the method of Claim 20 wherein the probes are labeled with nucleic acid analogs (Column 9, line 38-Column 10, line 10). Kurane et al do not teach the analogs are selected from the claimed analogs e.g. 2-amino purine. However, incorporation of 2-amino purine analogs into nucleic acid probes were well known in the art at the time the claimed invention was made as taught by Hawkins (Column 4, lines 44-54). Hawkins further teaches that fluorescent signals generated from probes comprising the 2-amino purine changes upon conformational change of the probe (Column 3, lines 26-36). It

would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the analog of Kurane et al with the 2-amino purine of Hawkins based on the teaching of Hawkins wherein conformational change produces a change in signal (Abstract).

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
June 12, 2003